

REMARKS

Claims 1-52 were pending in the subject application. Claims 7-9 have been cancelled as being confusing based on the reasons set forth for the claim objections of such claims on page 3 of the last Office Action. Claims 26 and 27 have been cancelled, without prejudice, as being redundant in view of the relevant amendments to claim 1. Claims 28-32 and 50 are cancelled as pertaining to nonelected subject matter. Claim 52 has been cancelled as being redundant in view of the relevant amendments to claim 1. Upon entry of the foregoing amendments, claims 1-6, 10-25, 33-49 and 51 will be before the Examiner for consideration.

The drawings have been rejected for certain informalities. New drawing sheets pertaining to FIG. 1A, 2A, 3A, 3B and 11 are submitted with this Amendment. Reconsideration is requested.

The Office Action clarifies that references listed in the application have not been considered as not being submitted in an IDS. Applicants submit that an IDS has been previously provided.

Claims 41-44 are objected to for being in improper form. Such claims have been amended to remove any confusing or apparent multiple dependency. Claim 35 depends from claim 1, and claims 41-44 depend from claim 35. Reconsideration is requested.

Claims 6, 25, 35, and 51 are objected to for various informal reasons. Such claims have been amended above which Applicant believes obviates this issue. Reconsideration is requested.

Claims 7-9 are objected to on the grounds that they do not further limit claim 1, the claim from which they ultimately depend. The amendments above obviate this issue. Claim 12 has been amended to remove the word leucoplast. As claim 1 is construed to contain leucoplasts, logically, claim 12, as amended, further limits claim 1. Claims 26 and 27 have been cancelled, which obviates the objection of such claims. Reconsideration of the related claim objections is requested.

Claims 9, 40, 45-46 are rejected under 35 USC § 112, first paragraph, as they are alleged to lack enablement. Applicants respectfully disagree. The office action takes the position that because the rejected claims refer to a specific tobacco variety, LAMD-609, and that this variety must be obtainable by a repeatable method or otherwise be readily available to the public. Applicants assert that LAMD-609 is a well known and widely available variety of tobacco. The variety was first characterized in 1974, See Collins, G. B., Legg, P. D. and Kasperbauer, M. C. (1974) Tobacco hybrid LAMD-609. *Crop Sci.*, 14, 72-80. Furthermore, the germplasm of the LAMD-609 variety is registered in *Crop Science*: M. K. Aycock, Jr. and C. L. Mulchi, *Registration of LAMD 609 Tobacco Germplasm*, *Crop Sci.* 1998 38: 904. Applicants assert that these references clarify and supports Applicant's position that the LAMD 609 tobacco variety is well known and obtainable. Based on these references and Applicant remarks, Applicant asserts that the rejected claims are enabled. Reconsideration of this rejection is respectfully requested.

Claims 4-5, 14, 16-17, 19, 25-27, 33-34, 45-49 and 51 are rejected under 35 USC § 112, second paragraph, as they are said to be indefinite. Applicants believe that the amendments to the rejected claims above obviate such grounds of rejection. It is noted that the amendments made to address the bases of rejection set forth under this rejection do not further limit the claims. In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration of this rejection.

Claims 1, 3-4, 7, 10, 12, 20, 23-27, 33 and 35-38 are rejected under 35 USC § 102(b), as being anticipated by McBride et al. Applicant respectfully traverses and otherwise asserts that the amendments to claim 1 obviate this rejection. Claim 1 has been amended to recite a DNA sequence coding for a IFNa2b or a polypeptide having at least 95 percent sequence identity therewith. Applicant will discussed in detail below in response to the obviousness rejections why they believe that the McBride et al. reference should be disqualified as prior art. However, with respect to this novelty rejection, Applicant asserts that the McBride et al. reference does not teach all of the elements of claim 1, as it does not teach the utilization of and the expression of a

IFNa2b encoding sequence. Applicant notes that this is acknowledged by the Examiner at page 14 of the office action evidenced by the Examiner's statement that McBride et al. in view of Chandrasegaran do not teach use of IFNa2b. In view of the fact that McBride et al. does not teach use of IFNa2b, McBride cannot anticipate claim 1, as it does not teach all of the elements of the claim. Furthermore, the other rejected claims, which ultimately depend from claim 1, are construed to contain all of the limitations of claim 1 and set forth additional distinguishing features. Therefore, it must be concluded that these dependent claims also are not anticipated by the McBride et al. reference. In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration of this 35 USC § 102(b) rejection.

Claims 1, 3-5, 7, 10-12, 15-17, 20, 23-27, 33, 35-38 and 47-49 are rejected under 35 USC 103(a) as being obvious over McBride et al. in view of Daniell. Applicant traverses, and otherwise respectfully asserts that the amendments to claim 1 obviate the grounds for this rejection. Applicant notes that claim 52 is not included under this rejection for the reason that neither McBride et al. nor Daniell teach the use of IFNa2b. Applicant notes that claim 1 has been amended to incorporate the limitations of claim 52. Thus, as a matter of straightforward logic, the amendments to claim 1 distinguish over the cited references and render claim 1 nonobvious over such cited references. Furthermore, the other rejected claims, which ultimately depend from claim 1, are construed to contain all of the limitations of claim 1 and set forth additional distinguishing features. Therefore, it must be concluded that these dependent claims also are not obvious over the McBride et al. and Daniell references. Reconsideration of this 35 USC 103(a) rejection is respectfully requested.

Claims 1, 3-5, 6-7, 10, 12-14, 18-20, 23-27, 33 and 35 are rejected under 35 USC 103(a) as being obvious over McBride et al. in view of Maliga et al. Applicant traverses. Additionally, Applicant respectfully asserts that the amendments to claim 1 obviate the grounds for this rejection. Applicant notes that claim 52 is not included under this rejection for the reason that neither McBride et al. nor Maliga et al. teach the use of IFNa2b. Applicant further notes that claim 1 has been amended to incorporate

the limitations of claim 52. Thus, as a matter of straightforward logic, the amendments to claim 1 distinguish over the cited references and render claim 1 nonobvious over such cited references. Furthermore, the other rejected claims, which ultimately depend from claim 1, are construed to contain all of the limitations of claim 1 and set forth additional distinguishing features. Therefore, it must be concluded that these dependent claims also are not obvious over the McBride et al. and Maliga et al. references. Reconsideration of this 35 USC 103(a) rejection is respectfully requested.

Claims 1-4, 7, 10, 12, 20, 23-27, 33, 35-38 and 51 are rejected under 35 USC 103(a) as being obvious over McBride et al. in view of Chandrasegaran. Applicant traverses, and otherwise respectfully asserts that the amendments to claim 1 obviate the grounds for this rejection. Applicant notes that claim 52 is not included under this rejection for the reason that neither McBride et al. nor Chandrasegaran teach the use of IFNa2b. Applicant further notes that claim 1 has been amended to incorporate the limitations of claim 52. Thus, as a matter of straightforward logic, the amendments to claim 1 distinguish over the cited references and render claim 1 nonobvious over such cited references. Furthermore, the other rejected claims, which ultimately depend from claim 1, are construed to contain all of the limitations of claim 1 and set forth additional distinguishing features. Therefore, it must be concluded that these dependent claims also are not obvious over the McBride et al. and Chandrasegaran references. Reconsideration of this 35 USC 103(a) rejection is respectfully requested.

Claims 1, 3-4, 7-8, 10, 12, 20, 23-27, 33, and 35-39 are rejected under 35 USC 103(a) as being obvious over McBride et al. in view of Conkling et al. Applicant traverses. In addition, Applicant respectfully asserts that the amendments to claim 1 obviate the grounds for this rejection. Applicant notes that claim 52 is not included under this rejection for the reason that neither McBride et al. nor Conkling et al. teach the use of IFNa2b. Applicant further notes that claim 1 has been amended to incorporate the limitations of claim 52. Thus, as a matter of straightforward logic, the amendments to claim 1 distinguish over the cited references and render claim 1 nonobvious over such cited references. Furthermore, the other rejected claims, which

ultimately depend from claim 1, are construed to contain all of the limitations of claim 1 and set forth additional distinguishing features. Therefore, it must be concluded that these dependent claims also are not obvious over the McBride et al. and Conkling et al references. Reconsideration of this 35 USC 103(a) rejection is respectfully requested.

Claims 9, 40 and 45-46 are rejected under 35 USC 103(a) as being obvious over McBride et al. in view of Conkling et al. and further in view of Aycock et al. Applicant traverses. Moreover, Applicant respectfully asserts that the amendments to claim 1 obviate the grounds for this rejection. Applicant notes that claim 52 is not included under this rejection for the reason that neither McBride et al. nor Conkling et al. nor Aycock et al. teach the use of IFNa2b. Applicant further notes that claim 1 has been amended to incorporate the limitations of claim 52. Thus, as a matter of straightforward logic, the amendments to claim 1 distinguish over the cited references and render claim 1 nonobvious over such cited references. Furthermore, the rejected claims, which ultimately depend from claim 1, are construed to contain all of the limitations of claim 1 and set forth additional distinguishing features. Therefore, it must be concluded that these dependent claims also are not obvious over the McBride et al., Conkling et al. and Aycock et al. references, as they do not teach or suggest all of the elements of the rejected claims. Reconsideration of this 35 USC 103(a) rejection is respectfully requested.

Claims 21-22 are rejected under 35 USC 103(a) as being obvious over McBride et al. in view of Daniell and further in view of Rathinasabapathi et al. Applicant traverses. Further, Applicant respectfully asserts that the amendments to claim 1 obviate the grounds for this rejection. Applicant notes that claim 52 is not included under this rejection for the reason that neither McBride et al. nor Daniell nor Rathinasabapathi et al. teach the use of IFNa2b. Applicant further notes that claim 1 has been amended to incorporate the limitations of claim 52. Thus, as a matter of straightforward logic, the amendments to claim 1 distinguish over the cited references and render claim 1 nonobvious over such cited references. Furthermore, the other rejected claims, which ultimately depend from claim 1, are construed to contain all of the

limitations of claim 1 and set forth additional distinguishing features. Therefore, it must be concluded that these dependent claims also are not obvious over the McBride et al., Daniell, and Rathinasabapathi et al. references. Reconsideration of this 35 USC 103(a) rejection is respectfully requested.

Claims 34 and 52 are rejected under 35 USC 103(a) as being obvious over McBride et al. in view of Chandrasegaran, and further in view of Reichert et al. At this time, Applicant will discuss the McBride et al. reference in further detail. As a starting point, it is a well established tenet in patent law that the prior art must enable a claimed invention in order to render it obvious. *Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 1551 (Fed. Cir. 1989), "Although published subject matter is "prior art" for all that it discloses, in order to render an invention unpatentable for obviousness, the prior art must enable a person of ordinary skill to make and use the invention." Applicant points out that a careful examination of the McBride et al. reference reveals that the McBride et al. reference does not sufficiently enable the use and/or plant based expression of interferon. Indeed, interferon is only mentioned once in the entire lengthy document, and that was only the inclusion in a group within a claim of possible things that could be expressed. It is interesting to note that the patent that ultimately issued from the McBride et al. reference (which is a patent publication) does not mention interferon even once. The one mention of interferon in the McBride patent application was removed from the case during examination. The McBride et al. contains no teaching or reference to sequence that encodes an interferon molecule. The McBride et al. reference contains no teaching of how to construct a vector that includes an interferon encoding sequence, nor the successful transformation of an interferon encoding vector. Moreover, the McBride et al. reference is devoid of any teaching of whether an interferon molecule can be successfully expressed, much less whether the interferon molecule can be properly processed and folded to result in an active protein.

The Chandrasegaran reference cannot cure the deficiencies of the primary McBride et al. reference. The Chandrasegaran reference teachings nothing about chloroplast transformation nor does it teach the use and/or expression of interferon.

The Chandrasegaran reference is cited for teaching of histidine tag and thrombin cleavage sites.

The Reichert et al. reference is cited merely for the purpose of illustrating that the sequence of IFN α 2b was known prior to the filing of the present application. Applicant does not dispute this. However, Reichert et al. teaches nothing about plant transformation, much less chloroplast transformation. As such, it is clear that the Reichert et al. reference cannot cure the above noted deficiencies of the primary McBride et al. reference.

It appears that the patent office may be trying to distill down this rejection to the rudimentary point that chloroplast transformation was known and IFN α 2b was known. Therefore, any known protein expressed in chloroplasts is obvious. Applicant takes great issue with this position. Using claim 1 as a starting point, the construction of a successful chloroplast vector that properly integrates into the plastid genome is only a first, but fundamental, step in the effort to express a never before expressed protein in chloroplasts. Expressing a foreign protein and protection from degradation, proper folding, etc. is a challenge with each new protein expressed in chloroplasts. Successful expression of a complex therapeutic protein in chloroplasts in higher plants was quite unpredictable before the teachings of the present application, especially as of the earliest priority date. Also, it should be pointed out that even if the foreign protein is properly expressed, it may be toxic to chloroplasts or cause sterility. There are several examples in the literature where foreign genes were successfully integrated into the chloroplast genome but were not expressed because of codon composition or degraded after expression or were found to toxic to chloroplasts or during reproduction, resulting in sterile plants. Furthermore, the amount of work that goes into successfully constructing a new vector; transforming cells, selecting for cells, identifying whether a given protein is expressed and then determining whether such protein is active is labor intensive, requires a great amount of skill, and is fraught with failures before successes. It cannot be reasonably asserted that just because one protein is known, that a vector

encoding such protein for chloroplasts will successfully integrate, express, and produce active protein.

In view of the foregoing remarks, Applicant respectfully asserts the position that the primary McBride et al. reference cannot be fairly said to fully enable the invention that is and was recited in claims 34 and 52, respectively. Moreover, the secondary references do not cure the significant deficiencies of the primary McBride et al. reference. Accordingly, Applicant respectfully requests reconsideration of this 35 USC 103(a) rejection.

Applicant acknowledges the provisional double patenting rejection set forth on pages 14 and 15 of the office action. Applicant requests that this rejection be held in abeyance until the indication of allowable subject matter in either this application or the application upon which the double patenting rejection is based. As a related point, there appears to be an error in the citation to the related application. The related application is listed as the application no. of the present application.

Applicants believe that they have fully and adequately addressed all of the rejections of record and urge that the pending claims are in a condition for allowance. Should the Examiner be of the opinion that any other issues remain, Applicant requests that the undersigned be contacted to arrange an interview to address any other outstanding issues.

Respectfully submitted,

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